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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,488	11/20/2003	Gregory D. Plowman	034536-0179	8719

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,488	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/20/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment, filed November 20, 2003 is acknowledged.

Claims 1-8 and 12-32 have been cancelled.

Claim 11 has been amended.

Claims 9-11 are pending and are under consideration in this application.

Priority

2. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Applicant's amendment to the first line of the specification, filed 11/20/2003, is acknowledged. However, this amendment fails to indicate the relationship of the instant

application to the earliest non-provisional application, U.S.S.N. 09/866,987 filed 5/30/2001. Applicant must amend the fist line of the specification to reflect the proper relationship.

It is also noted that priority is claimed to U.S. provisional application 60/208,291 filed on 05/30/2001, U.S. provisional application 60/246,974 filed on 11/13/2000, U.S. application 09/866,987 filed on 05/30/2001 and U.S. application 09/986,992 filed on 9/13/2001. The instant application, U.S.S.N. 10/716,488, and the parent application, U.S.S.N. 09/986,992 disclose that SEQ ID NO: 2, gene name SGP037, is 372 amino acids in length (see Table 1, page 101 of the instant specification). The two provisional applications both disclose SEQ ID NO: 43, gene name SGP037, but the polypeptide sequence is only 107 amino acids long.

No sequence corresponding to gene name SGP037 is contained in U.S.S.N. 09/866,987 (see Table 1, page 106 of the disclosure of U.S.S.N. 09/866,987). As such, the correct relationship of U.S.S.N. 09/986,992 to U.S.S.N. 09/866,987 should be a continuation in part. Clarification and/or correction are required.

Specification

3. The disclosure is objected to because of the following informalities:

A) The word immunochromatography is misspelled on page 53, line 24.

B) In Tables 1-4, pages 101, 103, 105, and 107, amino acid is misspelled.

C) On page 113, line 25, contain should be substituted for the current word "contains".

D) The last sentence of the paragraph from lines 17-27 of page 113 does not appear to be a complete sentence.

E) Many hyperlinks and/or other forms of browser-executable code have been found in the specification, such as lines 3 and 8 of page 45 and line 3 of page 48. These are impermissible and must be deleted. See MPEP § 608.01.

Appropriate correction of all of the above is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

4. Claim 11 is objected to because of the following informalities: The c in C terminal tail, recited in the last line of claim 11(i)(b), should be capitalized. Additionally, claim 11 would read more correctly if the word "has", recited in the first line of claim 11(i)(a), were changed to "is". Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is drawn to a hybridoma that produces the antibody of claim 9. The scope of claim 9 is such that it reads on both monoclonal and polyclonal antibodies that specifically bind a polypeptide comprising SEQ ID NO: 2. A hybridoma is not capable of producing polyclonal antibodies. Amending the claim to recite, for example, "A hybridoma which produces a monoclonal antibody that specifically binds a polypeptide consisting of SEQ ID NO: 2" would obviate this rejection.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 9-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicant has claimed and antibody that specifically binds a phosphatase polypeptide. Applicant has cloned a nucleotide sequence that encodes the polypeptide of SEQ ID NO: 2 (see particularly Example 1, pages 108-110). In claim 9 and the specification, Applicant has asserted that SEQ ID NO: 2 is a phosphatase.

Characterization of this sequence was carried out based on homology to other known and predicted proteins. This characterization indicated that SEQ ID NO: 2 is a serine-threonine phosphatase that belongs to the PP2C class of phosphatases, and that the most homologous molecule found in the public domain is a putative PP2C from the plant *Arabidopsis thaliana* (see page 48, lines 25-29, page 113, lines 12-27, page 114, lines 1-10, and GenBank sequence display for NP_197876). Applicant has described assays to test phosphatase activity (see page 121, lines 1-22) and to determine the polypeptides with which the phosphatase interacts (see page 122, line 17 to page 124, line 10). However, the specification does not appear to provide any indication that biochemical characterization of SEQ ID NO: 2 was performed to demonstrate that it is a phosphatase, nor does it indicate a ligand or ligands with which SEQ ID NO: 2 interacts.

The closest match to SEQ ID NO: 2 in the public database is a molecule translated from a plant nucleic acid clone that is predicted to be a PP2C, and applicant has not biochemically demonstrated that SEQ ID NO: 2 is a phosphatase or defined the substrates that are dephosphorylated by SEQ ID NO: 2. Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see particularly the Abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular

the Abstract and Box 2 on page 36). In the instant case, SEQ ID NO: 2 is only 35% identical to the putative plant PP2C (see page 114, line 10 of the instant specification). Thus, the homology-based assignment of SEQ ID NO: 2 as a PP2C does not appear to provide sufficient evidence of a specific and substantial utility for the polypeptide of SEQ ID NO: 2 based on the knowledge of the skilled artisan and the data presented in the instant specification. Therefore an antibody that is specific for the polypeptide of SEQ ID NO: 2 also lacks utility.

Additionally, even if for the sake of argument SEQ ID NO: 2 is a phosphatase, it would still lack a specific and substantial utility. Applicant has disclosed on page 51, lines 16-18, that antibodies to SEQ ID NO: 2 are useful in examining altered phosphatase expression in tissues. These antibodies can be immobilized, used *in vitro*, *in vivo*, *in situ*, in immunochromatography and in kits (see particularly page 53, lines 21-26). Altered levels of a phosphatase in a sample as compared to a normal control may indicate the presence of disease (see particularly page 54, lines 14-15), and numerous diseases are disclosed on page 59, lines 6-16. However, all of these utilities relate to anti-phosphatase antibodies in general and not to antibodies specific for the putative phosphatase of SEQ ID NO: 2.

The specification discloses that the phosphatase of SEQ ID NO: 2 is a member of the PP2C family of phosphatases based on homology, and indicates some of the signaling pathways associated with PP2C phosphatases in general on page 49, lines 14-23 of the instant specification. It does not appear that Applicant has disclosed any particular pathway with which the phosphatase of SEQ ID NO: 2 may be involved, and

no working examples are provided to demonstrate a physiological role for SEQ ID NO: 2.

The prior art indicates that PP2Cs function in multiple divergent biological pathways. Schweighofer et al. (Trends in Plant Science, 2004, 9:236-243, see entire document) indicate that one role of PP2Cs in eukaryotes is to reverse stress induced protein kinase cascades (see particularly page 239, left column, section titled PP2C functions in eukaryotes). In humans, PP2Cα inhibits the activation of p38 and JNK MAPK cascades, while PP2Cβ inactivates the TAK1 stress-signaling pathway (see particularly page 239, right column, the third and fourth paragraphs). As such, it is evident that PP2Cs are regulating diverse signaling pathways at different levels of the MAPK cascade (see the penultimate sentence of the fourth paragraph found in the right column of page 239 in particular). Evidence also exists that PP2C is involved in the dephosphorylation of the cystic fibrosis transmembrane conductance regulator (CFTR), as reported by Dahan et al. (Pflugers Archiv European Journal of Physiology, 2001, 443 Supplement 1:S92-S96, see entire document, particularly the section titled CFTR is dephosphorylated by membrane-bound PP2C; evidence for a regulatory complex, which begins on the right column of page S94). Therefore, the teachings of the prior art fail to disclose a specific biochemical pathway that is regulated by regulated by PP2Cs.

Since both the specification and the prior art appear to indicate multiple signaling pathways that include PP2Cs, a skilled artisan would not know what to do with the polypeptide of SEQ ID NO: 2, or an antibody specific for the polypeptide of SEQ ID NO:

2, without conducting additional research. Therefore, the claimed invention lacks a specific and substantial utility.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

11. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make use the invention of a kit containing an antibody that binds a polypeptide 90% identical to SEQ ID NO: 2 or that binds a polypeptide lacking one or more, but not all, of the domains of SEQ ID NO: 2.

Applicant has disclosed SEQ ID NO: 2, and has indicated in Table 3, page 105, that the phosphatase domain consists of amino acid residues 104 to 339 of SEQ ID NO: 2. Definitions for the other domains of the polypeptide listed in part (i)(a) of claim 11 can be found on pages 9-12 of the specification, and indicate a catalytic domain is

responsible for carrying out phosphate transfer reactions (see particularly page 9, lines 26-29). These definitions do not indicate where these domains are located in relation to the 372 amino acids of SEQ ID NO: 2, and some of them, such as a proline rich region, are defined in relative terms. The definition of a C terminal catalytic domain (see the paragraph that spans pages 10 and 11) is unclear, but it appears that SEQ ID NO: 2 does not contain a C terminal catalytic domain since SEQ ID NO: 2 contains 33 amino acid residues beyond the boundary of the catalytic domain.

Similarly, Applicant has indicated that polypeptides at least about 90% identical to SEQ ID NO: 2 are encompassed by the present invention, yet guidance appears to be lacking as to which regions of SEQ ID NO: 2 are amenable to mutation or what structure needs to be maintained to prevent the loss of function. The scope of the claim is very broad in that polypeptides that are at least about 90% identical to SEQ ID NO: 2 are not required to maintain any structure or function.

It is known in the art that assigning function based on homology is problematic, with the complexity of the problem rising as the similarity falls (see Whisstock et al., Quarterly reviews of Biophysics, 2003, 36:307-340, particularly the sentence that spans pages 321 and 323). Even single amino acid differences can result in drastically altered functions between two proteins, and as such only experimental evidence can confirm the function of a polypeptide (see Whisstock et al., particularly the first full sentence of page 323 and the last sentence of the conclusions of page 335). As such, it is known that alterations in the sequence of a polypeptide can lead to unpredictable changes in function.

Applicant has claimed an antibody that binds to a sequence that is at least about 90% identical to that of SEQ ID NO: 2, or binds a polypeptide lacking one or more, but not all, of the domains found in SEQ ID NO: 2. The intended use of these antibodies is in diagnostic assays (see particularly page 51, lines 16-18), and as indicated previously, the function of SEQ ID NO: 2 is unclear. Applicant has not indicated what, if any, activity needs to be maintained by a polypeptide that is at least about 90% identical to SEQ ID NO: 2. Additionally, it appears that no working example or guidance is provided as an aid in determining the region or regions of the polypeptide that are amenable to substitutions, insertions, deletions, or are suitable as fragments for inducing an immune response. Colman (Research in Immunology, 1994, 145:33-36) teaches that even single amino acid changes can completely disrupt the binding between an antibody and an antigen (see particularly the paragraph that starts in the right column of page 33). As such, it is not clear that an antibody specific for a polypeptide 90% identical to SEQ ID NO: 2 or that lacks one or more domains of SEQ ID NO: 2 would be useful in diagnostic assays to detect a disease.

In view of the lack of guidance or a working example in the specification, the breadth of the claim, and the unpredictability of the prior art, a skilled artisan would not reasonably know how to use an antibody that binds a polypeptide 90% identical to SEQ ID NO: 2 since it may not bind the native sequence protein, and a skilled artisan would not know how to make an antibody that binds a polypeptide lacking one or more, but not all, of the domains of SEQ ID NO: 2 since the boundaries and definitions of these domains are unclear. As such, skilled artisans would not be able to make the

antibodies of the claimed kit without undue experimentation.

12. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody that specifically binds a polypeptide consisting of SEQ ID NO: 2.

Applicant is not in possession of an antibody that binds either a polypeptide that is at least about 90% identical to SEQ ID NO: 2 or a polypeptide that lacks one or more, but not all domains present in SEQ ID NO: 2.

Applicant has claimed a genus of antibodies that binds to a sequence that is at least about 90% identical to that of SEQ ID NO: 2. SEQ ID NO: 2 is 372 amino acids, so 90% identity allows 37 residues to differ from SEQ ID NO: 2 by any of the 20 standard amino acids. Therefore, the genus of polypeptides at least about 90% identical to SEQ ID NO: 2 is at a minimum 37^{20} (about $2.3x10^{31}$), with the real number being even larger since the mutated residues are randomly distributed throughout the length of SEQ ID NO: 2. Adding in polypeptide fragments that lack one but not all domains of SEQ ID NO: 2 expands this number further, with only the species of SEQ ID NO: 2 being disclosed. Since many different antibodies can potentially bind a polypeptide sequence, the genus of antibodies is necessarily larger than the genus of

polypeptides. No antibodies specific for SEQ ID NO: 2 are disclosed as having been made.

No definition of the structure required by polypeptides derived from SEQ ID NO: 2 appears to be present in the specification. Without a definition of the structure of the polypeptides, it is impossible to describe the structural characteristics of the genus of antibodies that specifically bind polypeptides derived from SEQ ID NO: 2. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus of all antibodies that bind polypeptides at least about 90% identical to SEQ ID NO: 2 or a polypeptide that lacks one or more, but not all domains present in SEQ ID NO: 2. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. It is noted that claims 9-11 of the instant application may not have the benefit under 35 USC 120 of the filing date of U.S.S.N. 09/866,987 filed on 5/30/2001, or the benefit of the filing date under 35 USC 119(e) of U.S.S.N. 60/208,291 filed on 5/30/2000 or U.S.S.N. 60/246,974 filed on 11/12/2000. The scope of claims 9-11 of the instant application require the full 372 amino acids disclosed as SEQ ID NO: 2. The entirety of this sequence is not disclosed in U.S.S.N. 09/866,987, 60/208,291, or 60/246,974. As such, the effective filing date for claims 9-11 of the instant application is 9/13/2001, the

filing date of U.S.S.N. 09/986,992, since it contains the first disclosure of the entire sequence of SEQ ID NO: 2.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Meyers, U.S. Patent Application Publication US2002/0077463 (see entire document).

Meyers teaches a protein, identified as 16105, that is 100% identical to the first 329 amino acids of the claimed SEQ ID NO: 2 (see particularly the abstract and Figures 1a and 1b). Additionally, antibodies that specifically bind 16105, hybridomas that make such antibodies, and kits containing such antibodies, are disclosed and claimed (see particularly paragraphs 129 to 135, paragraph 244, claim 5, and claim 8. The sequence of 16105 is fully disclosed in provisional application 60/205,260, filed on 5/19/2000. Antibodies specific for protein 16105 would necessarily also recognize the claimed polypeptide of SEQ ID NO: 2, and since the domain of the polypeptide bound by the antibody is not recited, the prior art anticipates the claimed invention.

16. Claim 9 is rejected under 35 U.S.C. 102(e) as being anticipated by Roch et al., U.S. Patent Application Publication US2002/0106676 (see entire document).

Roch et al. disclose a polypeptide, PN7740, as SEQ ID NO: 4 and describe its cloning on page 10, paragraph 75. This sequence is 100% identical to the claimed SEQ ID NO: 2 of the instant application. The sequence of Roch et al. is fully disclosed in their provisional application 60/240,790 filed on 10/17/2000. Claims 50 and 51 of US2002/0106676 are directed toward an antibody that is specifically immunoreactive with a polypeptide comprising SEQ ID NO: 4 (PN7740) or with eight contiguous amino acids of SEQ ID NO: 4 (PN7740). Page 17, paragraph 117 discloses that polyclonal, monoclonal, and single chain antibodies are within the scope of the claimed invention. As such, the prior art anticipates the claimed invention.

17. Claims 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Au-Young et al., WO 01/96546 (see entire document).

Au-Young et al. teach a polypeptide sequence (SEQ ID NO: 1, identified as "PP-1") that is 100% identical to SEQ ID NO: 2 of the instant application, as well as monoclonal antibodies produced by hybridomas that specifically bind said polypeptide (see particularly lines 16-25 of page 26, lines 25-31 of page 7, page 42, line 21 to page 44 line 19, and claims 1, 10, 30, 31, 33, 36, 37, and 39-42). The entire 372 amino acids of PP-1 are disclosed in provisional application 60/212,447 filed on 6/16/2000. Therefore, the prior art anticipates the claimed invention.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roch et al. (U.S. Patent Application Publication US2002/0106676, see entire document) in view of Campbell (Monoclonal Antibody Technology, 1984, Elsevier Science Publishing Company Inc., Chapter 1, pages 1-32).

The teachings of Roch et al. have been discussed above. These teachings differ from the claimed invention in that they do not indicate the use of a hybridoma to make a monoclonal antibody that specifically binds SEQ ID NO: 2.

Campbell teaches the general properties and applications of monoclonal antibodies, and clearly indicates that monoclonal antibodies can be obtained from hybridomas (see entire document, particularly the first full paragraph of page 2 and Figure 1.1 on page 3). The advantage of using hybridomas for producing monoclonal antibodies is that unlike an isolated plasma cell that quickly dies in culture, a hybridoma cell is capable of both eternal growth and specific antibody production (see particularly the paragraph that spans pages 2 and 4).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a hybridoma as taught by Campbell to make the monoclonal antibody taught by Roch et al. Motivation for one of ordinary skill in the art at the time the invention was made to use hybridomas to make monoclonal antibodies comes from the advantage of unlimited cell growth coupled with specific antibody secretion that is a hallmark of hybridoma cells as taught by Campbell. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meyers (U.S. Patent Application Publication US2002/0077463, see entire document) in view of Zola (in *Current Protocols in Immunology*, 1998, 6.21.1 to 6.21.17).

The teachings of Meyers have been discussed above. They differ from the claimed invention in that Meyers does not disclose the use of a negative control antibody as part of the kit.

Zola teaches the importance of using negative control antibodies in scientific assays (see entire document, particularly the section titled Critical Parameters and Troubleshooting, pages 6.21.13 to 6.21.15). The advantage of using negative control antibodies is that they serve as a way to assess the validity of the experimental results, and as such they should be included in every test run (see particularly the paragraph that spans the left and right columns of page 6.21.14).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add a negative control antibody as taught by Zola to the kit taught by Meyers. Motivation for one of ordinary skill in the art at the time the invention was made to make this addition comes from the teaching of Zola that negative controls are needed to ensure that valid experimental tests are being performed. From the combined teachings of the references, it is apparent that one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

21. No claims are allowable.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
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November 15, 2004

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